Ciguatera poisoning: an unwelcome vacation experience

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A married couple in their late 50s traveled to Costa Rica on vacation. They both dined frequently on local fish. While in the country, they developed nausea, vomiting, and diarrhea, with up to 10 bowel movements per day. These symptoms were followed by tingling of the extremities and a sensation of "pricking by pins and needles" that was exacerbated by the movement of air over the skin. In addition, they reported a peculiar feeling of migratory alternating hot and cold sensations of the limbs. Fatigue, photophobia, and the perception of flashing lights were also reported. The gastrointestinal symptoms resolved after 1 week but other symptoms persisted for 3 months. After nonproductive visits to three different physicians, they sought additional consultation.

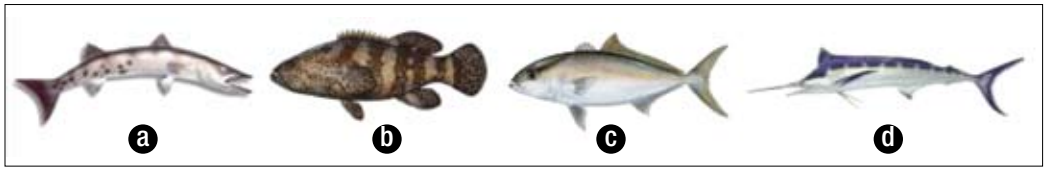

Figure. Fish particularly susceptible to *Gambierdiscus toxicus:* **(a)** barracuda, **(b)** grouper, **(c)** amberjack, **(d)** marlin.

Examinations were normal except for decreased vibratory and temperature sensation of the lower legs and hands. Their strength and reflexes were normal, as were results of a complete blood count, chemistry profile, sedimentation rate, urinalysis, and thyroid studies. Blood samples were sent to a research laboratory at the National Ocean Service in Charleston, South Carolina, and to the Center for Marine Science at the University of North Carolina at Wilmington. Microarray analysis for gene expression at both laboratories reported markers that were similar to samples from other patients with clinical diagnoses of ciguatera poisoning.

Amitriptyline was prescribed, and symptoms progressively diminished over a 3-week period, more so for the female than for the male. Their symptoms were still present 3 months after the institution of treatment but were minimal.

DISCUSSION

Ciguatera fish poisoning is caused by *Gambierdiscus toxicus,* the most common marine toxin on our planet. It is frequently unrecognized and misdiagnosed. At least 50,000 people per year are estimated to develop the disease, and this number is thought to represent only a fraction of actual cases. The Centers for Disease Control and Prevention estimated that only 2% to 10% of ciguatera cases are reported.

G. toxicus is found in association with algae that grow on coral reefs. Smaller herbivore fish acquire the toxin as they eat the algae. The toxin concentrates as it moves up the food chain when smaller affected fish are eaten by larger ones. Most cases in humans come from the consumption of large barracuda, grouper, amberjack, and marlin *(Figure).* Ingestion of barracuda fish is the most cited cause in the medical literature. None of the mentioned fish contain the toxin consistently. Contamination is dependent upon the presence of the toxin in the feeding waters, and this varies by location and also over time in local waters. Cold water fish, such as salmon, arctic char, rainbow trout, and halibut, are not exposed to the toxin. Ciguatera-infected fish look, smell, and taste normal, so identification is difficult.

The destruction and death of coral reefs allow for larger growths of the harboring algae. Reefs are fragile and easily damaged by hurricanes, military operations, commercial development, and possibly global warming. Damaged reefs are likely to increase future cases of ciguatera poisoning. Pollutants may also play a role. Algae growth is typically constrained because of scarce concentrations of nutrients. Nitrates and phosphates serve as nutrients for algae, and when their amounts are increased by pollution, rapid growth may ensue.

Ciguatera fish poisoning is endemic in temperate climates with reef systems. Low levels of *G. toxicus* are ubiquitous in such regions, but bloom numbers sufficient to cause disease are sporadic and unpredictable. Not all genetic strains are thought to produce the toxin and environmental triggers for toxin production are unknown, although some suspect that ocean pollutants may play a role.

Humans display consistent reactions when exposed to significant concentrations of *G. toxicus*. The toxin concentrates more in fish organs than in muscle tissues; thus, consumption of viscera

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can result in more severe illness. Ciguatera toxin acts on sodium channels in cell membranes, inducing membrane depolarization in nerve cells and striated muscle. The predominant symptoms come from the peripheral nervous system and can last for many months. Rare fatalities have been reported from respiratory paralysis. The toxin is not affected by heat or freezing. Avoiding fish that contain the toxin is the only preventive technique. To minimize exposure, it is recommended that smaller fish and smaller portions of different fish be chosen over larger portions of fish.

Most patients initially experience gastrointestinal tract symptoms that include diarrhea, nausea, and vomiting. These symptoms typically last just a few days and are followed by weakness and fatigue, with occasional hypotension or bradycardia. Dysthesias are the predominant and longest-lasting symptoms. Numbness is common, and the most striking and characteristic symptom is a peculiar disturbance in temperature sensation in which variable and sometimes alternating hot and cold feelings dance about the body. Some report an alteration of temperature sensation in which cold surfaces feel hot. In most patients neurological symptoms for the toxin abate within 6 months of onset.

The variable manner in which ciguatera toxin affects the nervous system has led to mistaken diagnoses of multiple sclerosis, chronic fatigue syndrome, chronic dermatitis, or psychiatric disorder. The hallmark findings of disordered temperature sensation are not always present.

Additional exposure to ciguatera toxin can exacerbate and prolong symptoms. It is recommended that affected individuals avoid suspect fish species for 6 months after resolution of the disease. Immunity to the toxin has not been recognized, and recurrences from additional exposure are often more pronounced than the initial illness.

Treatment of acute ciguatera poisoning has been successful and occasionally dramatic with intravenous mannitol. Ideally mannitol should be started within 72 hours of the ingestion of contaminated fish. Neurological symptoms have responded to amitriptyline and less favorably to gabapentin.

Confirmatory diagnostic tests have traditionally been difficult to obtain. Many island communities have been said to feed suspect fish to household pets or even elderly relatives to test for confirmation of symptoms. More scientific and less injurious to relatives and pets are radioimmune or enzyme-linked immunosorbent assays on suspect fish, though these are not readily available. More recently, polymerase chain reaction testing has been used to detect the toxin in blood samples of humans thought to be affected.

CONCLUSION

Ciguatera fish poisoning is increasing in frequency, and travel to temperate coastal locales and the importation of reef-dwelling fish increase the exposure of humans to this illness. The gastrointestinal and peripheral neurological symptoms associated with the toxin tend to be unique and typical—and thus potentially recognizable—yet the diagnosis is often not considered. Fish that harbor the toxin are unaffected and are unrecognizable in appearance or taste. It is thought that nearly all people who ingest sufficient concentrations of the toxin are susceptible to its effects. Early treatment may be effective, although avoidance of susceptible fish is the superior strategy. The diagnosis can be confirmed by testing the contaminated fish. While testing of human samples is beyond the scope of most laboratories, newer assays of DNA or RNA markers are in development and may allow for more rapid and reliable confirmation of the toxin from blood or tissue samples. Physicians should become familiar with the symptom complex that suggests the possibility of this disease.

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